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DIALOG(R) File 351:DERWENT WPI  
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003684135

WPI Acc No: 83-44112K/198319

XRAM Acc No: C83-043023

**Stabilisation of insulin solns. - by addn. of phospholipid, for use in continuous infusion devices**

Patent Assignee: NOVO IND AS (NOVO )

Inventor: BRANGE J J V; HANSEN P E; HAVELUND S

Number of Countries: 019 Number of Patents: 024

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
BE 894885	A	19830429					198319 B
GB 2107985	A	19830511	GB 8230978	A	19821029		198319
DE 3240177	A	19830511					198320
FR 2515517	A	19830506					198323
NL 8203944	A	19830516					198323
SE 8206168	A	19830530					198324
AU 8289861	A	19830505					198325
JP 58085815	A	19830523					198326
NO 8203603	A	19830524					198327
DK 8204791	A	19830627					198332
FI 8203702	A	19830630					198332
ZA 8207928	A	19830713					198344
PT 75766	A	19840412					198419
ES 8403025	A	19840601					198429
GB 2107985	B	19841114					198446
CH 649922	A	19850628					198530
CA 1198673	A	19851231					198606
AT 8203924	A	19860615					198630
US 4614730	A	19860930	US 84635485	A	19840731		198642
IT 1153315	B	19870114					198901
SE 460576	B	19891030					198946
JP 91066291	B	19911016	JP 82189335	A	19821029		199145
DE 3240177	C2	19930722	DE 3240177	A	19821029	A61K-037/26	199329
NL 193099	B	19980701	NL 823944	A	19821012	A61K-038/28	199831

Priority Applications (No Type Date): DK 823247 A 19820720; DK 814786 A 19811030

Patent Details:

Patent	Kind	Lan	Pg	Filing	Notes	Application	Patent
BE 894885	A		18				
DE 3240177	C2		7				

Abstract (Basic): BE 894885 A

Insulin solutions are stabilised by addn. of a phospholipid of formula (I) (where R1 and R2= H, alkylcarbonyl, alkenylcarbonyl, alkadienyl carbonyl, alkatrienyl carbonyl, or alkatetraenyl carbonyl, such that both R1 and R2 may not be H; R3= a hydrophilic group). The solutions may also contain zinc, a preservative, an agent to make the solution isotonic and a buffer.

The solns. are more resistant to interfacial polymerisation when at body heat than are known stabilised solutions of insulin. They are therefore more suitable for use in continuous infusion devices.

Title Terms: STABILISED; INSULIN; SOLUTION; ADD; PHOSPHOLIPID; CONTINUOUS;

INFUSION; DEVICE

Derwent Class: B04

International Patent Class (Main): A61K-037/26; A61K-038/28

International Patent Class (Additional): A61K-009/08; A61K-031/66;

A61K-047/00; C07C-103/52; C07F-009/09; C07F-009/10; C07G-000/00;

C07K-007/40

File Segment: CPI

Manual Codes (CPI/A-N): B04-B02D; B05-B01P; B12-M06; B12-M07

Chemical Fragment Codes (M1):

\*01\* F012 F014 F423 F521 G010 G013 G100 H1 H100 H101 H181 H182 H4 H401  
H441 H481 H8 J0 J011 J012 J1 J111 J171 J172 J3 J371 K0 K2 K224 L2  
L250 M280 M311 M312 M313 M314 M315 M320 M321 M322 M331 M332 M333  
M340 M342 M343 M349 M371 M381 M391 M392 M423 M431 M510 M520 M521  
M530 M531 M540 M620 M782 M903 R023 R052 V0 V621 V901 V902 V917 V922

Chemical Fragment Codes (M2):

\*02\* B415 B515 B701 B713 B720 B815 B831 G037 G563 H100 H181 H401 H402  
H403 H405 H464 H481 H482 H483 H721 H722 H723 J0 J011 J012 J013 J171  
J2 J271 J272 L722 M220 M222 M223 M224 M225 M226 M231 M232 M233 M262  
M273 M281 M282 M283 M312 M313 M321 M322 M332 M342 M343 M349 M381  
M383 M391 M392 M411 M431 M510 M520 M530 M540 M541 M782 M903 Q620  
R023 R052

Chemical Fragment Codes (M6):

\*03\* M903 Q620 R023 R052 R111 R232 R315

Derwent Registry Numbers: 1851-U

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DIALOG(R) File 351:DERWENT WPI

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000914278

WPI Acc No: 72-74449T/197247

**Insulin-protamine complexes - prepn from protamine and alkali or ammonium salts of insulin**

Patent Assignee: JACKSON R L (JACK-I); LILLY & CO ELI (ELIL )

Number of Countries: 014 Number of Patents: 018

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
DE 2219635	A						197247 B
NL 7205865	A						197247
BE 782651	A						197301
FR 2134658	A						197309
US 3758683	A						197339
ZA 7202243	A						197352
DD 100708	A						197401
GB 1385086	A	19750226					197509
US 3868358	A	19750225					197510
CH 566784	A	19750930					197543
CA 976085	A	19751014					197544
SU 508162	A	19760415					197649
RO 64387	A	19790329					198022
DE 2219635	B	19801127					198049
CS 7202923	A	19801031					198108
JP 48001116	A	19730109					198233
JP 82035185	B	19820727					198233
NL 178258	B	19850916					198541

Priority Applications (No Type Date): US 71139120 A 19710430

Abstract (Basic): DE 2219635 A

An insulin-protamine complex contains an alkali or ammonium salt of Zn-free insulin with protamine sulphate in the proportion of 0.2-1.5 mg protamine per 100 units insulin, pref. 0.4-0.8 mg protamine sulphate. The insulin salt is prepd. by crystallisation of insulin from NaOH or NH<sub>4</sub>OH soln. then concentrating in vacuo to obtain the Na or NH<sub>4</sub> salt practically free from Zn or heavy metals. Prepn. of the complex is by mixing isotonic solns. of the 2 components at pH 6.5-8.0 pref. 7.2-7.6, when a stable fine suspension of the complex is formed.

Title Terms: INSULIN; PROTAMINE; COMPLEX; PREPARATION; PROTAMINE; ALKALI; AMMONIUM; SALT; INSULIN

Derwent Class: B04

International Patent Class (Additional): A61K-017/02; A61K-027/00; A61K-037/26; C07C-102/00; C07C-103/00; C07G-007/00; C07K-007/40; C08G-015/00

File Segment: CPI

Manual Codes (CPI/A-N): B04-B02D; B04-B04A; B12-H05

Chemical Fragment Codes (M1):

\*01\* V621 V751 V752 V753 V754 M431 P816 M782 R051 R052 R000 M423 M902

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DIALOG(R) File 351:DERWENT WPI

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010383440

WPI Acc No: 95-284754/199538

XRAM Acc No: C95-128497

Isolation of insulin that is correctly post-translationally processed -  
by reacting proinsulin with a mercaptan in the presence of a chaotropic  
agent and purificn. after absorption to hydrophobic resin

Patent Assignee: HOECHST AG (FARH )

Inventor: GERL M; LUDWIG J; OBERMEIER R; SABEL W

Number of Countries: 023 Number of Patents: 012

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
EP 668292	A2	19950823	EP 95101748	A	19950209	C07K-014/62	199538 B
DE 4405179	A1	19950824	DE 4405179	A	19940218	C07K-014/62	199539
NO 9500592	A	19950821	NO 95592	A	19950217	C07K-014/62	199542
AU 9512288	A	19950831	AU 9512288	A	19950216	C12P-021/04	199543
CA 2142780	A	19950819	CA 2142780	A	19950217	C12P-021/06	199545
FI 9500699	A	19950819	FI 95699	A	19950216	C07K-000/00	199545
JP 7265092	A	19951017	JP 9528946	A	19950217	C12P-021/00	199550
EP 668292	A3	19960207	EP 95101748	A	19950209	C07K-014/62	199622
US 5663291	A	19970902	US 95389487	A	19950216	C07K-001/107	199741
SG 46683	A1	19980220	SG 968251	A	19950209	C07K-000/00	199822
EP 668292	B1	19980513	EP 95101748	A	19950209	C07K-014/62	199823
DE 59502138	G	19980618	DE 502138	A	19950209	C07K-014/62	199830
			EP 95101748	A	19950209		

Priority Applications (No Type Date): DE 4405179 A 19940218

Cited Patents: 2.Jnl.Ref; EP 37255; EP 379162; EP 600372

Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
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EP 668292	A2	G	16			
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Designated States (Regional): AT BE CH DE DK ES FR GB GR IE IT LI LU NL  
PT SE

DE 4405179	A1	13
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JP 7265092	A	10
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US 5663291	A	12
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EP 668292	B1	G 20
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Designated States (Regional): AT BE CH DE DK ES FR GB GR IE IT LI LU NL  
PT SE

DE 59502138	G	Based on	EP 668292
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Abstract (Basic): EP 668292 A

Claimed is a process for the isolation of correctly linked insulin  
by reacting (a) a protein of the formula R2-R1-B2-B29-Y-X-Gly-A2-A20-R3  
(II) in which X = amino acids Lys or Arg or a peptide with 2 to 35  
amino acids contg. Arg or Lys at the N-terminal and carboxyl end of the  
peptide Y = amino acid R1 = phenyl alanine residue or a covalent bond  
R2 = hydrogen, Arg or Lys, a peptide with 2 to 45 amino acids contg.  
Arg or Lys at the carboxyl end of the peptide, R3 = an amino acid  
residue, A2-A20 and B2 to B29 correspond to the amino acid sequence of  
the A or B chain respectively of human insulin, animal insulin or  
insulin derivs. with an mercaptan amt. resulting in 2 to 10 SH-residues  
of the mercaptan per cystein residue of formula (II) in the presence of  
a chaotropic auxiliary agent in an aq. medium at a pH of 10 to 11 and

protein concns. of 0.05 and 0.3 g/l, (b) reacting the proinsulin obtd. including correctly linked cystine bridges with either trypsin, trypsin-like protein or opt. also with carboxypeptidase B or a mixt. thereof for the prodn. of correctly folded insulin and (c) adding to the prod. of (b) 3 to 50 g of a hydrophobic absorber resin per litre of aq. medium at a pH of 4 to 7 and (d) isolating the absorber resin with absorbed insulin and e) eluting the insulin.

ADVANTAGE - Compared to prior art methods using proinsulin or insulin produced in E. coli, the new method requires fewer steps and has a greater yield.

Dwg.0/0

Abstract (Equivalent): US 5663291 A

A process for obtaining insulin of the formula (I), which comprises

A) reacting a protein of the formula II (SEQ ID NO:1)

R2-R1-B2-B29-Y-X-Gly-A2-A20-R3(II)

with an amount of a mercaptan which yields 2 to 10 -SH radicals of the mercaptan per cysteine residue of the protein of the formula II, in the presence of at least one chaotropic auxiliary in an aqueous medium at a pH of 10 to 11 and a concentration of the protein of the formula II of 0.05 to 0.3 g per litre of aqueous medium and

B) reacting the resulting pro-insulin having correctly linked cystine bridges with trypsin or a trypsin-like enzyme and optionally additionally with carboxypeptidase B or a mixture of the enzymes mentioned to give the insulin of the formula I having correctly linked cystine bridges,

C) treating the reaction product thus obtained with 3 to 50 g of a hydrophobic adsorber resin per litre of aqueous medium at a pH of 4 to 7,

D) isolating the adsorber resin containing adsorbed insulin of the formula I and

E) desorbing the insulin of the formula I from the adsorber resin; in this case, in formulae I and II

X is

a) an amino acid residue from the group consisting of Lys and Arg  
or

b) a peptide having 2 to 35 amino acid residues, containing the amino acid residue Arg or Lys at the N-terminal and carboxyl end of the peptide,

Y is a genetically encodable amino acid residue,

Z is

a) an amino acid residue from the group consisting of Lys and Arg,

b) a peptide having 2 or 3 amino acid residues, containing the amino acid residue Arg or Lys at the carboxyl end of the peptide or

c) OH,

R1 is a phenylalanine residue or a covalent bond,

R2 is

a) a hydrogen atom,

b) an amino acid residue from the group consisting of Lys and Arg

or

c) a peptide having 2 to 45 amino acid residues, containing the amino acid residue Arg or Lys at the carboxyl end of the peptide,

R3 is a genetically encodable amino acid residue and

the residues A2-A20 correspond to the amino acid sequence of the A chain of human insulin, animal insulin or an insulin derivative and the residues B2-B29 correspond to the amino acid sequence of the B chain of human insulin, animal insulin or an insulin derivative.

Dwg.0/0

Title Terms: ISOLATE; INSULIN; CORRECT; POST; PROCESS; REACT; PRO; INSULIN;  
MERCAPTAN; PRESENCE; AGENT; PURIFICATION; AFTER; ABSORB; HYDROPHOBIC;  
RESIN

Derwent Class: B04

International Patent Class (Main): C07K-000/00; C07K-001/107; C07K-014/62;  
C12P-021/00; C12P-021/04; C12P-021/06

International Patent Class (Additional): C07K-001/04; C07K-001/08;  
C07K-001/113; C07K-001/20; C07K-014/00; C12P-027/06

File Segment: CPI

Manual Codes (CPI/A-N): B04-J03A; B11-B

Chemical Fragment Codes (M1):

\*01\* D011 D601 F012 F014 F423 F521 G010 G013 G100 H1 H100 H101 H181 H182  
H4 H401 H441 H481 H5 H598 H8 H9 J0 J011 J012 J1 J111 J171 J172 J3  
J371 K0 K2 K224 L2 L250 M210 M211 M271 M280 M281 M311 M312 M313 M314  
M315 M320 M321 M331 M332 M333 M340 M342 M343 M349 M371 M381 M391  
M423 M510 M511 M520 M521 M530 M531 M540 M620 M903 M904 V0 V621 V902  
V917 V922 9538-05401-N

Generic Compound Numbers: 9538-05401-N

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DIALOG(R)File 351:DERWENT WPI

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009910012

WPI Acc No: 94-177718/199422

XRAM Acc No: C94-081244

Prod'n. of pro-insulin with correct disulphide bridges - by treating recombinant precursor protein with mercaptan in alkali and in presence of chaotropic agent, then isolation on hydrophobic resin

Patent Assignee: HOECHST AG (FARH )

Inventor: GERL M; LUDWIG J; OBERMEIER R; SABEL W

Number of Countries: 020 Number of Patents: 012

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
EP 600372	A1	19940608	EP 93118993	A	19931125	C07K-007/40	199422 B
AU 9352039	A	19940616	AU 9352039	A	19931130	C07K-007/40	199429
NO 9304357	A	19940603	NO 934357	A	19931201	C07K-007/40	199429
CA 2110442	A	19940603	CA 2110442	A	19931201	C07K-007/40	199431
FI 9305358	A	19940603	FI 935358	A	19931130	C07K-000/00	199431
JP 6228191	A	19940816	JP 93301480	A	19931201	C07K-007/40	199437
AU 662083	B	19950817	AU 9352039	A	19931130	C07K-007/40	199541
US 5473049	A	19951205	US 93160376	A	19931201	A61K-038/28	199603
EP 600372	B1	19970205	EP 93118993	A	19931125	C07K-014/62	199711
DE 59305396	G	19970320	DE 505396	A	19931125	C07K-014/62	199717
			EP 93118993	A	19931125		
ES 2097426	T3	19970401	EP 93118993	A	19931125	C07K-014/62	199720
SG 46612	A1	19980220	SG 966726	A	19931125	C07K-000/00	199822

Priority Applications (No Type Date): DE 4240420 A 19921202

Cited Patents: 2.Jnl.Ref; EP 347781; EP 489780; WO 9103550

Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
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EP 600372	A1	G	15			
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Designated States (Regional): AT BE CH DE DK ES FR GB IE IT LI NL SE

JP 6228191	A		9			
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AU 662083	B			Previous Publ.		AU 9352039
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US 5473049	A		8			
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EP 600372	B1	G	15			
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Designated States (Regional): AT BE CH DE DK ES FR GB IE IT LI NL SE

DE 59305396	G			Based on		EP 600372
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ES 2097426	T3			Based on		EP 600372
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Abstract (Basic): EP 600372 A

Prod'n. of pro-insulin of formula (I) comprises (1) reacting protein R2-R1-B2-B29-Y-X-Gly-A2-A20-R2 (II) with a mercaptan (III) to provide 2-10 SH residues per Cys residue in (II), in presence of a chaotropic agent and in aq. medium of pH 10-11, with (II) concn. 0.05-0.3 g/l; (2) the (I) produced is treated with 3-50 g hydrophobic adsorber resin per l aq. medium at pH 4-7; (3) the resin plus adsorbed (I) is isolated and (4) (I) is desorbed; where X is genetically encoded aminoacid (AA) or peptide of 2-35 AA residues; Y is genetically encoded AA; R1 is Phe or covalent bond; R2 is H, genetically encoded AA or peptide of 2-45 AA residues; R3 is genetically encoded AA; residues A2-A20 and B2-B29 correspond to the AA sequences of A and B chains of human or animal insulin or of an insulin deriv..

USE/ADVANTAGE - (I) is a precursor of insulin. This method produces (I) from genetically engineered (II) with correctly bonded Cys bridges. Compared with known methods it involves fewer stages (esp. no sulphitolysis or cyanogen bromide cleavage) and overall losses during purification are reduced, i.e. the process is quicker and gives better yields. Complete redn. of (II) is not necessary and, despite the presence of large amts. of contaminating proteins, refolding yields are comparable to those for purified (I) having SH protecting gps.. (I) can be enzymatically converted to insulin directly after desorption, without intermediate isolation or purification..

Dwg.0/0

Abstract (Equivalent): EP 600372 B

A process for obtaining proinsulin of the formula (I), which comprises (A) reacting a protein of the formula R1-R1-B2-B29-Y-X-Gly-A2-A20-R3 (II) with a quantity of a mercaptan, which quantity yields 2 to 10 -SH radicals of the mercaptan per cysteine residue of the protein of the formula II, in the presence of at least one chaotropic auxiliary agent in an aqueous medium at a pH of 10 to 11 and at a concentration of the protein of the formula II of 0.05 to 0.3 g per litre of aqueous medium, and the proinsulin of the formula I which is obtained, (B) being mixed with 3 to 50 g of a hydrophobic adsorber resin per litre of aqueous medium at a pH of 4 to 7, (C) the adsorber resin; which has adsorbed proinsulin of the formula I, being isolated, and (D) the proinsulin of the formula I being desorbed from the adsorber resin; in formula I and II, X is (a) a genetically encodable amino acid residue or (b) a peptide possessing 2 to 35 amino acid residues, Y is a genetically encodable amino acid residue, R1 is a phenylalanine residue or a covalent bond, R2 is (a) a hydrogen atom, (b) a genetically encodable amino acid residue, or (c) a peptide possessing 2 to 45 amino acid residues, R3 is a genetically encodable amino acid residue, and the residues A2-A20 correspond to the amino acid sequence of the A chain of human insulin, animal insulin, or an insulin derivative, and the residues B2-B29 correspond to the amino acid sequence of the B chain of human insulin, animal insulin, or an insulin derivative.

Dwg.0/0

Abstract (Equivalent): US 5473049 A

A process for obtaining proinsulin of the formula I which comprises (A) reacting a protein of the Formula II: R2-R1-B2-B29-Y-X-Gly-A2-A20-R3(II) with a quantity of a mercaptan, which quantity yields 2 to 10 -SH radicals of the mercaptan per cysteine residue of the protein of the Formula II, in the presence of at least one chaotropic auxiliary agent in an aqueous medium at a pH of 10 to 11 and at a concentration of the protein of the Formula II of 0.05 to 0.3 g per liter of aqueous medium, and the to form a reaction mixture;  
(B) mixing the reaction mixture with 3 to 50 g of a hydrophobic adsorber resin per liter of aqueous medium at a pH of 4 to 7, to form the proinsulin of the Formula I;  
(C) isolating the adsorber resin, which has adsorbed proinsulin of the Formula I; and  
(D) desorbing the proinsulin of the Formula I from the adsorber resin;  
wherein in Formula I and II  
X is a) a genetically encodable amino acid residue or b) a peptide having 2 to 35 amino acid residues,  
Y is a genetically encodable amino acid residue,



R1 is a phenylalanine residue or a covalent bond,  
R2 is a) a hydrogen atom, b) a genetically encodable amino acid  
residue or c) a peptide having 2 to 45 amino acid residues,  
R3 is a genetically encodable amino acid residue, and  
the residues A2-A20 correspond to the amino acid sequence of the A  
chain of human insulin, and the residues B2-B29 correspond to the amino  
acid sequence of the B chain of human insulin.

Dwg.0/0

Title Terms: PRODUCE; PRO; INSULIN; CORRECT; DI; SULPHIDE; BRIDGE; TREAT;  
RECOMBINATION; PRECURSOR; PROTEIN; MERCAPTAN; ALKALI; PRESENCE; AGENT;  
ISOLATE; HYDROPHOBIC; RESIN

Derwent Class: A96; B04

International Patent Class (Main): A61K-038/28; C07K-000/00; C07K-007/40;  
C07K-014/62

International Patent Class (Additional): A61K-037/26; C07K-001/04;  
C07K-001/113; C07K-001/14; C07K-003/08; C07K-017/08; C07K-099/26;  
C07K-099-26; C12N-015/17

File Segment: CPI

Manual Codes (CPI/A-N): A12-W11D; A12-W11L; B04-C01G; B04-J03A

Chemical Fragment Codes (M1):

\*01\* F012 F014 F423 F521 G010 G013 G100 H100 H101 H181 H182 H4 H441 H481  
H498 H598 J0 J011 J012 J111 J171 J172 J371 K0 K2 K224 L250 M210 M211  
M271 M280 M281 M311 M312 M313 M314 M315 M321 M331 M332 M333 M340  
M342 M343 M349 M371 M381 M391 M423 M510 M520 M521 M530 M531 M540  
M720 M903 M904 N131 N135 N425 V621 V902 V914 V915 V916 V917 V922  
9422-07401-P

Polymer Indexing (PS):

<01>

\*001\* 017; R00708 G0102 G0022 D01 D02 D12 D10 D19 D18 D31 D51 D53 D58 D88  
; H0000; H0011-R; M9999 M2073; P1741 ; P1752

\*002\* 017; H0022 H0011; G0851 G0840 G0817 D01 D02 D12 D10 D19 D18 D31 D51  
D54 D58 D90; R00708 G0102 G0022 D01 D02 D12 D10 D19 D18 D31 D51 D53  
D58 D88; M9999 M2073; P1741 ; P1774

\*003\* 017; ND01; B9999 B3383-R B3372; B9999 B3509 B3485 B3372; Q9999  
Q7750; Q9999 Q8059 Q7987

Generic Compound Numbers: 9422-07401-P

6/9/1

DIALOG(R) File 351:DERWENT WPI

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007796762

WPI Acc No: 89-061874/198909

XRAM Acc No: C89-027329

Isolation of basic proteins from protein mixts. - using strongly acidic cation exchange column and eluting with a water-alcohol mixt.

Patent Assignee: HOECHST AG (FARH )

Inventor: DORSCHUG M; OBERMEIER R; DOERSCHUG M; OBERMEIER R

Number of Countries: 013 Number of Patents: 019

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
DE 3726655	A	19890223	DE 3726655	A	19870811		198909 B
EP 305760	A	19890308	EP 88112661	A	19880804		198910
AU 8820591	A	19890216					198915
NO 8803554	A	19890306					198915
DK 8804476	A	19890212					198918
FI 8803708	A	19890212					198918
JP 1086896	A	19890331	JP 88198127	A	19880810		198919
HU 47958	T	19890428					198923
ZA 8805871	A	19890426	ZA 885871	A	19880810		198924
PT 88230	A	19890630					198930
US 5101013	A	19920331	US 88230085	A	19880809		199216
IL 87385	A	19930818	IL 87385	A	19880809	C07K-001/14	199340
EP 305760	B1	19931027	EP 88112661	A	19880804	C07K-003/22	199343
DE 3885214	G	19931202	DE 3885214	A	19880804	C07K-003/22	199349
			EP 88112661	A	19880804		
ES 2047007	T3	19940216	EP 88112661	A	19880804	C07K-003/22	199411
FI 91875	B	19940513	FI 883708	A	19880809	C07K-001/14	199422
NO 175004	B	19940509	NO 883554	A	19880810	C07K-007/40	199422
PH 26874	A	19921116	PH 37374	A	19880809	C07K-007/40	199635
JP 2587867	B2	19970305	JP 88198127	A	19880810	C12P-021/02	199714

Priority Applications (No Type Date): DE 3726655 A 19870811

Cited Patents: 1.Jnl.Ref; A3...9023; DD 247684; EP 439; EP 87932; FR 2375193; GB 2173503; No-SR.Pub

Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
DE 3726655	A		5			
EP 305760	A	G				
US 5101013	A		5			
EP 305760	B1	G	8			
DE 3885214	G			Based on		EP 305760
ES 2047007	T3			Based on		EP 305760
FI 91875	B			Previous Publ.		FI 8803708
NO 175004	B			Previous Publ.		NO 8803554
JP 2587867	B2		4	Previous Publ.		JP 1086896

Abstract (Basic): DE 3726655 A

Isolation of basic proteins from protein mixts. obtd. by enzymatic cleavage of proinsulin and/or its derivs. of natural, semisynthetic or gene technological origin comprises charging the protein mixt. to a strongly acidic cation exchange column, and eluting with a water/1-4C alcohol mixt. contg. 10-50% (pref. 20-40%, esp. 30%) of the alkanol.

USE/ADVANTAGE - Proinsulin is a precursor in the biosynthesis of

human insulin. The process enables the sepn. of insulin of basic character to relatively easily. Derivatisation of the proteins during sepn. is avoided. Aggregation of the sepd. proteins does not occur. The exchange column can be reused without problems. (5pp Dwg.No.0/2)

Abstract (Equivalent): EP 305760 B

A process for the isolation of basic proteins from a protein mixture which contains such basic proteins and which has been obtained by enzymatic cleavage of proinsulin and/or one of its derivatives of natural, semisynthetic or genetic engineering origin by loading an ion exchanger with the protein mixture and elution, which comprises using a strongly acid cation exchanger as the ion exchanger and carrying out the elution by means of an H<sub>2</sub>O/Cl-C<sub>4</sub>-alkanol mixture which contains about 10 to 50%, preferably about 20 to 40% and in particular about 30% of alkanol.

Dwg.0/2

Abstract (Equivalent): US 5101013 A

Process for the isolation of basic proteins from a protein mixt. comprises (a) loading a strongly acid cation exchanger with the protein mixt. and (b) eluting the proteins using water and a 1-4C alkanol mixt. of 10-50% vol. of alkanol. The pH of the eluting soln. is 2.5-5.5 and (a) is carried out at pH 3.5-4.0. Pref. the eluting soln. contains ethanol or isopropanol as the 1-4C alkanol and a buffer e.g. an organic acid esp. lactic acid. The elution is carried out with an ammonium or alkali metal salt gradient of 0-1 (pref. 0.15-0.35) mol/l. Pref. the strongly acid cation exchanger contains sulphopropyl gps.

USE/ADVANTAGE - Used for the isolation of basic proteins from a protein mixt. contg. basic proteins obtd. by enzymatic cleavage of proinsulin, or a natural, semi-synthetic or genetically engineered deriv. Better sepn. and isolation of the proteins is obtd. and additional derivatisation of the proteins during the sepn. is avoided. Only a small amt. of alkanol is required and exchangers are reusable.

()

Title Terms: ISOLATE; BASIC; PROTEIN; PROTEIN; MIXTURE; STRONG; ACIDIC; CATION; EXCHANGE; COLUMN; ELUTION; WATER; ALCOHOL; MIXTURE

Derwent Class: B04

International Patent Class (Main): C07K-001/14; C07K-003/22; C12P-021/02

International Patent Class (Additional): B01J-039/04; C07K-001/18;

C07K-003/20; C07K-005/00; C07K-007/40; C07K-013/00; C07K-014/62;

C07K-015/04; C07K-099/26; C12P-021/00

File Segment: CPI

Manual Codes (CPI/A-N): B04-B02D3; B04-B04A6; B11-B

Chemical Fragment Codes (M1):

\*01\* M423 M720 M903 N161 N421 V621 V752

5/9/1

DIALOG(R)File 351:DERWENT WPI

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007173982

WPI Acc No: 87-170991/198725

XRAM Acc No: C87-071241

XRPX Acc No: N87-128339

Thermoplastic moulding compsn. resistant to leakage currents, etc. -  
contains halogenated co-polycarbonate, graft polymer, TFE polymer,  
antimony or bismuth cpd., titanium dioxide, etc.

Patent Assignee: BAYER AG (FARB )

Number of Countries: 008 Number of Patents: 004

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
DE 3544295	A	19870619	DE 3544295	A	19851214		198725 B
EP 229956	A	19870729	EP 86116929	A	19861205		198730
JP 62141059	A	19870624	JP 86291678	A	19861209		198731
US 4731405	A	19880315	US 86935824	A	19861128		198814

Priority Applications (No Type Date): DE 3544295 A 19851214

Cited Patents: DE 2211826; EP 131751; FR 2223422

Patent Details:

Patent	Kind	Lan	Pg	Filing	Notes	Application	Patent
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DE 3544295	A		6				
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EP 229956	A	G					
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Designated States (Regional): DE ES FR GB IT NL

US 4731405	A		6				
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Abstract (Basic): DE 3544295 A

Compsns. (I) comprise: A. 60-85 wt.% copolycarbonate, contg. 3-20 wt.% halogen, of a dihydric phenol and a dihydric halogenated phenol; B. 10-30 wt.% graft polymer of: 1) 5-90 wt.% mixt. of: a. 50-95 wt.% styrene, alpha-methylstyrene, nuclearly substd. styrene, and/or MMA, and b. 50-5 wt.% (meth)acrylonitrile, MMA, maleic anhydride, and/or N-substd. maleimide, on 2) 95-10 wt.% acrylate rubber of max. glass temp. (Tg) 10 deg.C; C. 5-30 wt.% thermoplastic copolymer of: 1) 50-95 wt.% styrene, alpha-methylstyrene, nuclearly substd. styrene, and/or MMA; and 2) 50-5 wt.% (meth)acrylonitrile, MMA, maleic anhydride, and/or N-substd. maleimide, where % under A, B, and C total 100; D. 0.05-2.0 pts.wt., A + B + C, TFE polymer, average particle size 100-1000 microns, density 2.0-2.3 g/cub. cm; E. 1-5 pts.wt., per 100 pts.wt. A + B + C, Sb2O3, Sb carbonate, Bi2O3, or Bi carbonate; F. 4-12 pts.wt., per 100 pts.wt. A + B + C, TiO2, and opt. G. 0-15 pts.wt., per 100 pts.wt. A + B + C, lower mol. organic halogen cpd. where halogen content of A + G does not exceed 20 wt.% A + G.

USE/ADVANTAGE - Partic. injection moulding, to form household articles (e.g., juice presses); covering panels for building trade; parts for motor vehicle mfr.; electrical engineering (e.g., switch boxes); also deep drawing of sheets or films. (I) have good resistance to leakage currents, flames, and heat, good processability; mouldings have acceptable surface quality after exposure to leakage currents.

Abstract (Equivalent): US 4731405 A

Thermoplastic moulding material comprises (A) 60-85 pts. wt. copolycarbonate contg. 3-20 wt.% halogen, of a divalent-phenol and a divalent halogenated phenol, (B) 10-30 pts. wt. graft polymer of (1)

5-90 pts. wt. mixt. of (i) 50-95 wt.% styrene, alpha-methylstyrene, nuclear-substd. styrene or methyl methacrylate and (ii) 50-5 wt.% (meth)acrylonitrile, methyl methacrylate maleic anhydride or N-substd. maleimide or (2) 95-10 pts. wt. acrylate rubber having Tg up to 10 deg.C, (C) 5-30 pts. wt. thermoplastic copolymer from (1) 50-95 wt.% styrene, alpha-methylstyrene, nuclear-substd. styrene- or methyl methacrylate and (2) 50-5 wt.% (meth)acrylonitrile, methyl methacrylate, maleic anhydride or N-substd. maleimide; (D) 0.05-2.0 pts. wt. TFE polymer having density 2.0-2.3 g/cm<sup>3</sup> and mean particle dia. 100-1000 micron; (E) 1-5 pts. wt. Bi or Sb trioxide, or carbonate, (F) 4-12 pts. wt. TiO<sub>2</sub>; and (G) 0-15 pts. wt. low mol. organic halogen cpd..

(A) + (B) + (C) totals 100. (D)-(G) are w.r.t. 100 pts. wt. (A) + (B) + (C). Halogen content resulting from (A) + (G) does not exceed 20 wt.% relative to total wt. of (A) + (G).

USE/ADVANTAGE - The compsn. has good flame resistance, tracking resistance, thermal stability and processability. Mouldings have acceptable surface quality after subjection to tracking current. Used for prod. of switch panels, multipoint etc..

Title Terms: THERMOPLASTIC; MOULD; COMPOSITION; RESISTANCE; LEAK; CURRENT; CONTAIN; HALOGENATED; CO; POLYCARBONATE; GRAFT; POLYMER; TFE; POLYMER; ANTIMONY; BISMUTH; COMPOUND; TITANIUM; DI; OXIDE

Index Terms/Additional Words: PTFE; POLY; TETRA; FLUOROETHYLENE

Derwent Class: A13; A14; A23; E32; Q22; V03; X27

International Patent Class (Additional): B62D-029/04; C08J-003/20;

C08K-003/22; C08K-013/02; C08L-025/00; C08L-027/18; C08L-033/00;

C08L-051/06; C08L-069/00

File Segment: CPI; EPI; EngPI

Manual Codes (CPI/A-N): A04-C01A; A04-D03A; A04-D08; A04-E08A; A04-E09;

A04-F05; A04-F06B; A05-E06A; A07-A04D; A08-F; A08-F02; A08-M09A; A08-R;

A09-A03; E31-M; E35-K02; E35-M

Manual Codes (EPI/S-X): V03-B04A; X27-B03

Plasdoc Codes (KS): 0003 0004 0007 0009 0016 0031 0037 0038 0207 0208 0210

0218 0222 0224 0072 0159 0162 0226 0299 0300 0306 0307 3160 3161 0320

0321 0376 0377 0383 0384 0489 0496 3035 0500 0502 0503 3011 3013 3014

0531 0535 0537 0538 0947 1093 1096 1292 1365 1367 1369 1373 1375 1417

1418 2218 2223 2224 2225 2237 2274 2281 2315 2330 2332 2334 2464 2465

2513 2522 3243 2545 2552 2553 2560 2597 2600 2645 2651 2655 2667 2679

2691 2737 2743 2756 3300 2829

Polymer Fragment Codes (PF):

\*001\* 014 02& 030 032 034 037 038 040 045 051 055 056 058 062 064 07& 072

074 075 076 077 08& 081 082 087 09& 104 105 106 117 122 143 15- 151

155 157 158 18- 19& 213 217 218 219 220 221 27& 27- 28& 308 310 311

312 314 318 321 329 331 339 392 393 394 396 400 42& 42- 43- 435 437

44& 44- 456 459 461 476 502 506 51& 510 511 512 539 541 57& 575 580

592 593 597 604 608 613 623 627 637 672 688 721 722

Chemical Fragment Codes (M3):

\*01\* A351 A383 A422 A940 C108 C550 C730 C801 C802 C803 C804 C805 C807

M411 M781 M903 M904 M910 Q010 Q020 Q030 Q130 Q606 R038 R043 R01501-U

R01527-U R01966-U

\*02\* A351 A383 A940 C106 C108 C530 C730 C801 C802 C803 C805 C807 M411

M781 M903 M904 Q010 Q020 Q030 Q130 Q606 R038 R043 R12464-U R12465-U

Derwent Registry Numbers: 1501-U; 1527-U; 1527-U; 1966-U; 1966-U

Specific Compound Numbers: R01501-U; R01527-U; R01966-U; R12464-U; R12465-U

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DIALOG(R) File 351:DERWENT WPI

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007160821

WPI Acc No: 87-157830/198723

Related WPI Acc No: 87-186353

XRAM Acc No: C87-065912

**Fusion proteins contg. interleukin 2 aminoacid sequences - as well as genes coding for these proteins, vectors contg. the genes, and host cells contg. the vectors**

Patent Assignee: HOECHST AG (FARH )

Inventor: HABERMANN P; WENGENMAYE F; WENGENMYER F; WENGENMAYER F

Number of Countries: 023 Number of Patents: 032

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
DE 3541856	A	19870604	DE 3541856	A	19851127		198723 B
EP 227938	A	19870708	EP 86116140	A	19861121		198727
AU 8665693	A	19870604					198729
NO 8604759	A	19870622					198730
JP 62143696	A	19870626	JP 86281621	A	19861126		198731
FI 8604798	A	19870528					198735
ZA 8608943	A	19870525	ZA 868943	A	19861126		198735
HU 43642	T	19871130					198751
DK 8605685	A	19870528					198801
PT 83813	A	19871130					198802
EP 464867	A	19920108	EP 91114412	A	19861121		199202
EP 468539	A	19920129	EP 91114411	A	19861121		199205
EP 227938	B	19920415	EP 86116140	A	19861121		199216
DE 3684892	G	19920521	DE 3684892	A	19861121	C12P-021/02	199222
			EP 86116140	A	19861121		
DK 9200522	A	19920421	DK 865685	A	19861126	C07K-013/00	199231
			DK 92522	A	19920421		
FI 9205312	A	19921123	FI 864798	A	19861125	C07K-000/00	199308
			FI 925312	A	19921123		
ES 2032378	T3	19930216	EP 86116140	A	19861121	C12P-021/02	199320
FI 9304079	A	19930917	FI 925312	A	19921123	C12N-000/00	199349
			FI 934079	A	19930917		
IL 80755	A	19931208	IL 80755	A	19861125	C07K-015/00	199408
FI 93471	B	19941230	FI 864798	A	19861125	C12N-015/62	199506
NO 176481	B	19950102	NO 864759	A	19861126	C07K-014/00	199507
EP 464867	B1	19950510	EP 86116140	A	19861121	C12N-015/62	199523
			EP 91114412	A	19861121		
DE 3650322	G	19950614	DE 3650322	A	19861121	C12N-015/62	199529
			EP 91114412	A	19861121		
ES 2073081	T3	19950801	EP 91114412	A	19861121	C12N-015/62	199537
EP 468539	B1	19950913	EP 91114411	A	19861121	C12N-015/15	199541
DE 3650396	G	19951019	DE 3650396	A	19861121	C12N-015/15	199547
			EP 91114411	A	19861121		
ES 2077747	T3	19951201	EP 91114411	A	19861121	C12N-015/15	199604
FI 97239	B	19960731	FI 925312	A	19921123	C12N-015/62	199639
			FI 934079	A	19930917		
KR 9500300	B1	19950113	KR 869990	A	19861126	C12N-015/00	199645
JP 2566933	B2	19961225	JP 86281621	A	19861126	C12P-021/02	199705
DK 172064	B	19971006	DK 865685	A	19861126	C07K-014/62	199747
DK 172210	B	19980105	DK 865685	A	19861126	C07K-014/815	199809
			DK 92522	A	19920421		

Priority Applications (No Type Date): DE 3541856 A 19851127

Cited Patents: A3...8847; EP 155655; EP 158198; EP 158564; EP 171024; EP 211299; No-SR.Pub

Patent Details:

Patent	Kind	Lan	Pg	Filing	Notes	Application	Patent
DE 3541856	A		20				
EP 227938	A	G					
Designated States (Regional): AT BE CH DE ES FR GB GR IT LI LU NL SE							
EP 464867	A						
Designated States (Regional): AT BE CH DE ES FR GB GR IT LI LU NL SE							
EP 468539	A						
Designated States (Regional): AT BE CH DE ES FR GB GR IT LI LU NL SE							
EP 227938	B	G	27				
Designated States (Regional): AT BE CH DE ES FR GB GR IT LI LU NL SE							
DE 3684892	G			Based on			EP 227938
DK 9200522	A			Div ex	DK 865685		
FI 9205312	A			Div ex	FI 864798		
ES 2032378	T3			Based on			EP 227938
FI 9304079	A			Div ex	FI 925312		
FI 93471	B			Previous Publ.			FI 8604798
NO 176481	B			Previous Publ.			NO 8604759
EP 464867	B1	G	9	Related to	EP 86116140		
Designated States (Regional): AT BE CH DE ES FR GB GR IT LI LU NL SE							
DE 3650322	G			Based on			EP 464867
ES 2073081	T3			Based on			EP 464867
EP 468539	B1	G	10				
Designated States (Regional): AT BE CH DE ES FR GB GR IT LI LU NL SE							
DE 3650396	G			Based on			EP 468539
ES 2077747	T3			Based on			EP 468539
FI 97239	B			Div ex	FI 925312		
				Previous Publ.			FI 9304079
JP 2566933	B2		18	Previous Publ.			JP 62143696
DK 172064	B			Previous Publ.			DK 8605685
DK 172210	B			Div ex	DK 865685		
				Previous Publ.			DK 9200522

Abstract (Basic): DE 3541856 A

Fusion proteins in which the C- or N-terminal essentially corresponds to the first 100 units of interleukin 2 are new. Also new are gene structures coding for the above fusion proteins, vectors containing these gene structures, and host cells containing these vectors. Hirudin derivs. with an amino acid sequence beginning N-terminally with Pro are new and claimed. Human interleukin 2 derivs. contg. Asp. C-terminally are new and claimed.

USE/ADVANTAGE - The new fusion proteins are of use in the prodn. of biologically active interleukin 2 (IL2) sequences by genetic engineering techniques. The fusion proteins are stable towards the host cells proteases, and are poorly soluble to insoluble and therefore easy to separate from soluble proteins by centrifugation. The new hirudin and human interleukin 2 derivs. are products by cleavage of the fusion proteins which both have better biological activity than the parent cpds. attributable to resistance to host organism proteases.

Abstract (Equivalent): EP 468539 B

A hirudin derivative which has an amino-acid sequence starting at the N terminus with Pro-His or Pro-Thr.

Dwg.0/3

EP 464867 B

A fusion protein which is composed of human interleukin-2 (IL-2) and hirudin and which exhibits both IL-2 activity and hirudin activity.

Dwg.0/2

EP 227938 B

A process for the prepn. of a fusion protein, which comprises expression in a host cell of a gene which codes for a C- pr N-terminal section which essentially corresponds to the first 100 aminoacids of interleukin-2 (IL-2), but does not have interleukin-2 activity. ( )u

Abstract (Equivalent): US 5496924 A

A fusion protein comprises a ballast portion and a desired protein, the ballast portion forming the N-terminus of the fusion protein and the ballast portion consisting essentially of residues of the amino acid sequence of interleukin-2 (IL-2), wherein the ballast portion contains at least a 22-residue amino acid sequence of IL-2 and lacks IL-2 biological activity in the T-cell proliferation test.

Dwg.0/22

Title Terms: FUSE; PROTEIN; CONTAIN; INTERLEUKIN; AMINOACID; SEQUENCE; WELL ; GENE; CODE; PROTEIN; VECTOR; CONTAIN; GENE; HOST; CELL; CONTAIN; VECTOR

Derwent Class: B04; D16

International Patent Class (Main): C07K-000/00; C07K-013/00; C07K-014/00; C07K-014/62; C07K-014/815; C07K-015/00; C12N-000/00; C12N-015/00; C12N-015/15; C12N-015/62; C12P-021/02

International Patent Class (Additional): C07G-017/00; C07H-021/04; C07K-001/12; C07K-003/08; C07K-007/40; C07K-014/55; C07K-015/04; C07K-015/06; C07K-019/00; C12N-001/20; C12N-001/21; C12N-015/09; C12N-015/17; C12N-015/26; C12N-015/63; C12N-015/70; C12P-019/34; C12P-021/00; C12R-001/19; C12P-021/02; C12R-001-19; C12R-001-645

File Segment: CPI

Manual Codes (CPI/A-N): B04-B04A1; B04-B04A5; B04-C01G; D05-C11; D05-C13

Chemical Fragment Codes (M1):

\*01\* M423 M710 M903 N135 Q233 V753

\*02\* D011 D601 F012 F014 F423 F521 G010 G013 G100 H1 H100 H101 H181 H182  
H4 H401 H441 H481 H498 H5 H598 H8 H9 J0 J011 J012 J1 J111 J171 J172  
J3 J371 K0 L2 L250 M210 M211 M271 M280 M281 M311 M312 M313 M314 M315  
M320 M321 M331 M332 M333 M340 M342 M343 M349 M371 M381 M391 M423  
M510 M511 M520 M521 M530 M531 M540 M620 M710 M903 N135 Q233 V752  
V901 V917 V921



3/9/1

DIALOG(R) File 351:DERWENT WPI

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007037978

WPI Acc No: 87-037975/198706

XRAM Acc No: C87-015952

**Fusion protein contg. sequence from the E. coli trp operon - and corresp. gene structures and vectors, esp. for prodn. of eucaryotic protein**

Patent Assignee: HOECHST AG (FARH )

Inventor: HABERMANN P; STENGELIN S; WENGENMAYE F; WENGENMAYER F

Number of Countries: 023 Number of Patents: 018

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
DE 3526995	A	19870205	DE 3526995	A	19850727		198706 B
EP 211299	A	19870225	EP 86109945	A	19860719		198708
AU 8660565	A	19870129					198710
JP 62029600	A	19870207	JP 86176558	A	19860726		198711
NO 8603000	A	19870223					198714
DK 8603554	A	19870128					198716
ZA 8605556	A	19870126	ZA 865556	A	19860725		198718
FI 8603041	A	19870128					198719
PT 83065	A	19870918					198741
HU 43629	T	19871130					198751
ES 2000278	A	19880201	ES 86544	A	19860724		198916
EP 211299	B	19900228					199009
DE 3669175	G	19900405					199015
IL 79522	A	19910816					199144
NO 175640	B	19940801	NO 863000	A	19860725	C07K-007/10	199430
CA 1336329	C	19950718	CA 514682	A	19860725	C12N-015/62	199536
JP 95113040	B2	19951206	JP 86176558	A	19860726	C07K-019/00	199602
KR 9500299	B1	19950113	KR 866142	A	19860726	C12N-015/00	199645

Priority Applications (No Type Date): DE 3526995 A 19850727

Cited Patents: 3.Jnl.Ref; A3...8822; EP 20147; EP 36776; No-SR.Pub

Patent Details:

Patent	Kind	Lan	Pg	Filing	Notes	Application	Patent
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DE 3526995	A		19				
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EP 211299	A	G	26				
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Designated States (Regional): AT BE CH DE FR GB IT LI LU NL SE

EP 211299	B	G					
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Designated States (Regional): AT BE CH DE FR GB IT LI LU NL SE

NO 175640	B			Previous Publ.		NO 8603000	
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JP 95113040	B2		19	Based on		JP 62029600	
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Abstract (Basic): DE 3526995 A

Fusion proteins of formula Met-Xn-D'-Y-Z (I) are new, where n = 0 or 1; X = sequence of 1-12 genetically codable amino acids; D' = sequence of about 70 amino acids from the 23-93 sequence of the D peptide in the trp operon of E. Coli; Y = sequence of one or more codable amino acids which facilitates the cleavage of downstream sequence Z; Z = sequence of codable amino acids.

Also new are (1) gene structures coding for (I); (2) vectors contg. such structures and (3) expression systems (esp. C. coli cells) contg. such vectors.

Pref. n = 1; X = N-terminal Lys-Ala; Y = (or contains) C-terminal

Met, Cys, Trp, Arg or Lys; Z = amino acid sequence of human proinsulin or a hirudin.

USE/ADVANTAGE - (I) can be easily isolated as ppt. and can be converted to the eucaryotic protein by enzymatic or chemical cleavage of Z.

0/11

Abstract (Equivalent): EP 211299 B

A fusion protein of the general formula

Met-Xn-D'-Y-Z

in which n is zero or 1, X is a sequence of 1 to 12 genetically codable amino acids, D' is a sequence of about 70 amino acids in the region of the sequence of amino acids 23-93 of the D-peptide in the trp operon of E.coli, Y denotes a sequence of one or more genetically codable amino acids which permits the following amino acid sequence Z to be cleaved off, and Z is a sequence of genetically codable amino acids. (26pp)

Title Terms: FUSE; PROTEIN; CONTAIN; SEQUENCE; COLI; OPERON; CORRESPOND; GENE; STRUCTURE; VECTOR; PRODUCE; EUKARYOTIC; PROTEIN

Index Terms/Additional Words: ESCHERICHIA

Derwent Class: B04; D16

International Patent Class (Main): C07K-007/10; C07K-019/00; C12N-015/00; C12N-015/62

International Patent Class (Additional): C07G-017/00; C07H-021/04; C07K-003/08; C07K-007/40; C07K-013/00; C07K-015/04; C07K-015/12; C12N-001/20; C12N-001/21; C12N-015/09; C12N-015/31; C12N-015/70; C12P-019/34; C12P-021/00; C12P-021/02; C12P-021/06; C12R-001/19

File Segment: CPI

Manual Codes (CPI/A-N): B04-B02B1; B04-B04A; B04-B04A1; B04-C01G; D05-H03B; D05-H12

Chemical Fragment Codes (M1):

\*01\* D011 D601 F012 F014 F423 F521 G013 G100 H1 H100 H101 H181 H182 H401  
H441 H481 H498 H5 H598 H9 J0 J011 J012 J1 J171 J172 J371 L250 M210  
M211 M271 M280 M281 M311 M312 M313 M314 M315 M320 M321 M331 M332  
M333 M340 M342 M343 M349 M371 M381 M391 M423 M510 M511 M520 M521  
M530 M531 M540 M620 M710 M903 Q233 V752 V901 V917 V921

\*02\* M423 M710 M903 Q233 V500 V540 V753

2/9/1

DIALOG(R) File 351:DERWENT WPI

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004623035

WPI Acc No: 86-126378/198620

XRAM Acc No: C86-053887

**Cleavage of peptide(s) and protein(s) - at methionyl bond using cyanogen chloride**

Patent Assignee: HOECHST AG (FARH )

Inventor: BICKER R; SEIPKE G

Number of Countries: 023 Number of Patents: 016

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
EP 180920	A	19860514	EP 85113857	A	19851031		198620 B
AU 8549713	A	19860515					198627
JP 61115096	A	19860602	JP 85249148	A	19851108		198628
DE 3440988	A	19860710	DE 3440988	A	19841109		198629
DK 8505164	A	19860510					198632
FI 8504383	A	19860510					198636
ZA 8508603	A	19860522	ZA 858603	A	19851108		198636
PT 81445	A	19860814					198639
US 4644057	A	19870217	US 85795920	A	19851107		198709
ES 8701780	A	19870301	ES 548617	A	19851107		198715
CA 1247081	A	19881220					198904
EP 180920	B	19920102					199202
DE 3585078	G	19920213					199208
DK 166546	B	19930607	DK 855164	A	19851108	C07K-003/00	199328
KR 9307428	B1	19930810	KR 858387	A	19851109	C07K-001/14	199431
JP 95014960	B2	19950222	JP 85249148	A	19851108	C07K-001/12	199512

Priority Applications (No Type Date): DE 3440988 A 19841109

Cited Patents: 1.Jnl.Ref; A3...8902; No-SR.Pub

Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
EP 180920	A	G	9			
Designated States (Regional): AT BE CH DE FR GB IT LI LU NL SE						
EP 180920	B					
Designated States (Regional): AT BE CH DE FR GB IT LI LU NL SE						
DK 166546	B			Previous Publ.		DK 8505164
JP 95014960	B2		3	Based on		JP 61115096

Abstract (Basic): EP 180920 B

Cleavage of peptides and proteins at the methionyl bond using cyanogen chloride (Cl-CN) is new.

Pref. the reaction medium is pref. a mixt. of water and a water-miscible acid, pref. formic acid, aq. 50-95 vol.% formic acid being particularly pref. ClCN is pref. used in a 2- to 20-fold (especially 5- to 8-fold) molar excess, per methionyl bond to be cleared. Reaction time is pref. 1-10 hrs.; especially 3-6 hrs. After the reaction, excess ClCN is pref. removed from the reaction mixt. using a suitable gas, pref. N<sub>2</sub>.

ADVANTAGE - Cyanogen chloride is easier and safer to use than cyanogen bromide (which has previously been used for the clearance of methionyl bonds in high yields.) In particular, as a gas ClCN is easier to measure and transport around the reaction system the solid BrCN.  
(9pp Dwg.No.0/9)

Abstract (Equivalent): EP 180920 B

A process for the cleavage of peptides and proteins at the methionyl bond, which comprises carrying out the cleavage with cyanogen chloride. (5pp)

Abstract (Equivalent): US 4644057 A

Peptides and proteins are cleaved at the methionyl bond by using cyanogen chloride (I).

Pref. excess (I) is removed, after reaction is complete, from the reaction mixt. using a suitable gas pref. nitrogen; and then the reaction mixt. is worked up as usual. Pref. (I) is used in 2-30-fold pref. 5-8-fold molar excess per methionyl bond to be cleaved. Pref. the reaction is effected in 1-10, esp. 3-6 hours. Pref. the reaction medium used is water and 50-95% by vol. of formic acid.

ADVANTAGE - (I) can be metered and conveyed more simply and safely than solid cyanogen bromide. (3pp)n

Title Terms: CLEAVE; PEPTIDE; PROTEIN; METHIONYL; BOND; CYANOGEN; CHLORIDE

Derwent Class: B04; D16

International Patent Class (Main): C07K-001/12; C07K-001/14; C07K-003/00

International Patent Class (Additional): C07C-000/00; C07G-000/00;

C07K-001/107; C07K-015/00; C07K-017/00; C12N-009/38; C12N-011/02;

C12N-015/00; C12P-001/04; C12P-021/00

File Segment: CPI

Manual Codes (CPI/A-N): B02-V03; B04-B02C3; B04-B02D2; B04-B02D4; B04-B04A;

B04-C01; B05-C03; B11-B; D05-H13

Chemical Fragment Codes (M1):

\*01\* F012 F014 F423 F521 G010 G013 G100 H1 H100 H101 H182 H4 H401 H441  
H481 H8 J0 J011 J012 J1 J111 J171 J172 J3 J371 K0 K224 L2 L250 M280  
M311 M312 M313 M314 M315 M320 M321 M322 M331 M332 M333 M340 M342  
M343 M349 M371 M381 M391 M392 M423 M510 M520 M521 M530 M531 M540  
M620 M720 M903 N209 N231 N309 N341 N361 N421 N512 Q233 V621 V902  
V917 V922

\*02\* M421 M423 M720 M903 N209 N231 N309 N341 N361 N421 N512 Q233 V275  
V624 V752

Derwent Registry Numbers: 0246-S; 1303-S

1/9/1

DIALOG(R) File 351:DERWENT WPI

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002564962

WPI Acc No: 80-82986C/198047

**Stabilised aq. solns. of protein, esp. insulin - contg. surfactant, pref. polyether, to prevent denaturation**

Patent Assignee: HOECHST AG (FARH )

Inventor: THUROW H

Number of Countries: 016 Number of Patents: 012

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Main IPC	Week
EP 18609	A	19801112					198047 B
FI 8001361	A	19801230					198105
JP 55157518	A	19801207					198107
DK 8001851	A	19810302					198113
DE 2952119	A	19810709					198129
CA 1146069	A	19830510					198321
EP 18609	B	19830921					198339
DE 3064888	G	19831027					198344
IL 59933	A	19840629					198432
US 4783441	A	19881108					198847
JP 89018920	B	19890407					198918
US 4885164	A	19891205					199006

Priority Applications (No Type Date): DE 2952119 A 19791222; DE 2917535 A 19790430

Cited Patents: DE 2212695; DE 2620483; DE 2641819; US 4179337; 3.Jnl.Ref

Patent Details:

Patent	Kind	Lan	Pg	Filing Notes	Application	Patent
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EP 18609	A	G				
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Designated States (Regional): AT BE CH DE FR GB IT LI NL SE

EP 18609	B	G				
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Designated States (Regional): AT BE CH DE FR GB IT LI NL SE

Abstract (Basic): EP 18609 A

Aq. protein solns. contain a surfactant (I) with a linear structure consisting of alternate weakly hydrophobic and weakly hydrophilic regions. Pref. (I) is a homopolymer, copolymer or block copolymer of formula (Ia)  $R_2Y-(X)_n-R_3$  (Ia) ((X)<sub>n</sub> is a chain of n members of formula -CHR<sub>1</sub>CHR<sub>1</sub>O- or -CHR<sub>1</sub>O- in any order; n is 2-80, pref. 8-45; Y is O or NH; R<sub>1</sub> is H, Me or Et, but must be Me or Et in at least half the gps. X; R<sub>2</sub> and R<sub>3</sub> are H or organic gps.). The solns., esp. insulin solns., are stabilised against denaturation of the protein, which can affect its immunological and biological properties. (I) prevents the adsorption of the protein on surfaces and hence prevents sec. reactions such as aggregation. The solns. may be used for therapeutic purposes (e.g. as insulin solns. with depot action), or for treating hydrophobic surfaces to prevent their adsorbing and denaturing effect on proteins, e.g. during the prepn. and purificn. of proteins, esp. by chromatography or ultrafiltration.

Title Terms: STABILISED; AQUEOUS; SOLUTION; PROTEIN; INSULIN; CONTAIN; SURFACTANT; PREFER; POLYETHER; PREVENT; DENATURE

Derwent Class: A25; A96; B04

International Patent Class (Additional): A61K-035/12; A61K-037/02; A61K-039/00; C07C-103/52; C07G-007/00; C07K-001/00; C07K-003/00;

C07K-007/40; C07K-099/26; C09K-015/14

File Segment: CPI

Manual Codes (CPI/A-N): A10-E08A; A10-E18; A12-V01; A12-W12C; B04-B02D;  
B04-B04A; B04-C03C; B12-H05; B12-M06; B12-M07; B12-M09

Plasdoc Codes (KS): 0002 0013 0231 1279 1588 1590 1592 1602 1604 1606 1630  
1632 1634 2000 2002 2014 2509 2571 2705 2706 2733 2766 2769

Polymer Fragment Codes (PF):

\*001\* 011 028 034 036 039 04- 147 157 198 200 231 24& 240 27& 31- 336 37-  
398 525 532 533 535 57- 623 624 642 643 645 688 720 721 726

Chemical Fragment Codes (M1):

\*01\* V621 V751 V752 V753 V754 V743 G100 M531 H141 H181 H182 H183 J171  
J172 J173 H541 H543 H581 H583 H584 H589 M620 H721 M240 M232 M233  
M331 M333 M431 M510 M520 M530 M540 P816 M782 Q620 R023 R024 Q616  
M423 M902